



IMPORTANCE OF FUROSEMIDE IN THE KIDNEY DISEASE – A REVIEW

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ABSTRACT

Furosemide is a loop diuretic, which is mostly used in different stages of kidney disease, it has many clinical roles. This review summarises the importance of furosemide and its efficacy in kidney disease. It is a potent natriuretic drug, that inhibits the Na⁺-K⁺-2Cl co-transporter to decrease the extracellular fluid volume expansion in heart and kidney disease. In patients with Heart failure, kidney disease, Lung disease furosemide is used to maintain the liquid balance to prevent or reduce edema. In treatment of hypertension also, furosemide is used. Lasix is the mostly preferred brand of furosemide. It helps in reduction of absorbing more amount of salt in our body which is later passed by urine. Its diuretics effect is determined by the urinary concentrations. Furosemide is considered as proxy because of its good urinary response in severity of acute kidney injury and due to some residual renal action. In CKD volume and sodium overload is corrected by furosemide. In kidney furosemide is fastly and completely excreted. In uric acid levels also furosemide has important role.

KEYWORDS: Furosemide, Loop diuretic, Acute kidney injury, Natriuretic drug, Edema, Chronic kidney disease.

INTRODUCTION

Furosemide is a loop diuretic, which is mostly used in different stages of kidney disease, it has many clinical roles. The importance of furosemide and its efficacy in kidney disease is more. It is a potent natriuretic drug, that inhibits the Na⁺-K⁺-2Cl co-transporter to decrease the extracellular fluid volume expansion in heart and kidney disease. In patients with Heart failure, kidney disease, Lung disease furosemide is used to maintain the liquid balance to prevent or reduce edema. In treatment of hypertension also, furosemide is used. Lasix is the mostly preferred brand of furosemide. It helps in reduction of absorbing more amount of salt in our body which is later passed by urine. Its diuretics effect is determined by the urinary concentrations. Furosemide is considered as proxy because of its good urinary response in severity of acute kidney injury and due to some residual renal action. In CKD volume and sodium overload is corrected by furosemide.^[1] Oral route and IV route is Furosemide is available and can be given by both routes but their bioavailability is different. Loop diuretic is an Anthranilic derivative so it helps to maintain the blood pressure and heart problems Like other drugs Furosemide also has some side-effects in CKD and hypertension patients. To avoid the consequences the effect of furosemide should be completely known. Correct dosage form of furosemide should be given to get therapeutic effect.^[2] It reduces the extracellular fluid

and increase the sodium excretion.^[3] It may sometimes damage the kidney more and improper sodium balance.^[10] The effect of Furosemide is more than mannitol.^[1]

MECHANISM OF ACTION

The loop diuretics examples like Furosemide, Bumetanide, and Torsemide which acted along the ascending limb and macula Densa that act by blocking the Na-K-2CL cotransporter from the lumen. It is a organic Anions, it interacts to Chlorine binding site in which by binding on transport protein that is within translocation pocket. When compared to Chlorine it is very large through pocket it's not transported which also helps in blocking the transporter. Distal convoluted Tubulediuretics example thiazides and thiazide like drugs which works above manner are some examples of organic anions but along the Distal convoluted Tubule which binding to thiazide sensitive NaCl cotransporter and their effect will be from the luminal side of the Tubule.^[4] The Sodium chloride which is filtered entering through the ascending loop of Henle into the cells. Luminal chloride concentration may also affects macula densa. The luminal NkCC2 is blocked by loop diuretics. This may also cause raising of intraglomerular pressure and renin secretion also increased. At macula densa the reabsorption of sodium chloride is blocked.^[5]

DIURETICS ACTING ON LOOP OF HENLE

In natriuresis the diuretics such as loop diuretics are very useful and shows good effect in acute condition but increased sodium reabsorption is observed in chronic condition. Loop diuretics limiting their volume of distribution and they (>90%) bound to proteins. Bioavailability of loop diuretic such as Furosemide on oral absorption ranges between 10% and 100% when we compared average will be 50%. It's absorption can be reduced by bowel edema when we congested patients but peak plasma will be at lower concentrations.^[5]

Dosing of diuretics is different for different patients and Furosemide which is a loop diuretic which is given for chronic kidney disease will be given at lower doses for patients if dialysis is not necessary for them.^[6] If extracellular fluid volume is increased, stage 3 to stage 5 is considered as chronic kidney disease then for treating hypertension priority will be given to loop diuretic.^[7] Because in CKD overloading of volume and sodium can be corrected by loop diuretics. If patient is taking high salt and by uremic anions effects sometimes in CKD sodium and volume overload can not be corrected by loop diuretics.^[8] Sodium transport proteins will be blocked in the apical plasma membrane of Kidney by the diuretics.^[9]

FUROSEMIDE IN NEONATES

The infants which are born preterm may suffer from immature renal function and improper tubular and Glomerular function.^[10] Furosemide is used to treat renal impairment and also pulmonary edema in infants. But mostly intravenous is preferred than oral.^[12]

ACUTE KIDNEY INJURY

Acute kidney injury is a disease with mortality and morbidity. AKI is caused due to infection, hypovolemia, cardiac insufficiency, and aminoglycosides antibiotics and radiocontrast agents. Furosemide used in many patients to treat AKI who are at risk. Reduction of portal hypotension and glomerular filtration increased is by furosemide. Furosemide has more effectiveness than mannitol.^[1]

CHRONIC KIDNEY DISEASE

Chronic Kidney Disease is common problem. If estimated Glomerular filtration rate is decreased below 60ml/min/1.73 m² or if urinary albumin to creatinine ratio is equal or exceeded 30mg/g for 3 months or more then is diagnosed as Chronic Kidney Disease. Common problem seen in CKD is edema which results solute excretion. So in CKD Furosemide is preferred. The damage of renal system which results in impairment of salt and water clearance which causes edema and overloading of fluid. To increase the water and salt clearance diuretic is used for treatment mostly mostly high potency diuretic is used.^[11] In loop diuretic furosemide is mostly used in this condition. Bumetanide and torsemide are other loop diuretics can be used because of high oral bioavailability than furosemide but

they are more costly than furosemide.^[13] Some patients when changed from Furosemide may have improved diuresis.

DIURETIC IN RENAL IMPAIRMENT

Renal impairment is related to heart failure and mortality is predicted by not depending. The drugs given for Renal impairment may have interactions with heart and may cause heart failure so by considering heart failure Renal impairment treatment is given. If beta blockers and Renin-Angiotension system blockade or SGLT2 inhibitor is given with Diuretic may cause hypotension and hypovolemia in such condition diuretic dose should be reduced to avoid it.^[14]

CONCLUSION

The current evidence suggests that furosemide is very much useful and helps to increase the improvement of renal function and decreases mortality. In lung disease also furosemide used to avoid fluid retention to increase mechanical ventilation. Furosemide is mostly used in mild AKI but not mostly in severe AKI. Diuretic drugs are used in case of decreased decreased renal function or in kidney damage. Loop diuretics usage helps in decongestion but it also precipitating AKI simultaneously. So Furosemide is best drug of choice for Renal impairment.

REFERENCES

1. Ho KM, Power BM. Benefits and risks of furosemide in acute kidney injury. *Anaesthesia*, 2009; 65: 283-93.
2. Saad A. Pharmacological Parameters Study on Loop Diuretic Drug—Furosemide. *Journal Of Formulation Science & Bioavailability*, 2018; 2(1): 117.
3. Diniah MN, Rachmawati H, Hasmono D, Kusumaningtyas AP. Furosemide use in chronic kidney disease patients. *KnE Medicine*, 2022 Sep 15: 60-74.
4. Ellison DH. Clinical pharmacology in diuretic use. *Clinical Journal of the American Society of Nephrology*, 2019 Aug 7; 14(8): 1248-57.
5. Palazzuoli A, Ruocco G, Ronco C, McCullough PA. Loop diuretics in acute heart failure: beyond the decongestive relief for the kidney. *Critical Care*, 2015 Dec; 19: 1-7.
6. Flythe JE, Assimon MM. Diuretic Use Among Patients Receiving Hemodialysis in the United States. *Kidney Medicine*, 2022 Sep 1; 4(9).
7. Roush GC, Sica DA. Diuretics for hypertension: a review and update. *American journal of hypertension*, 2016 Oct 1; 29(10): 1130-7.
8. Minutolo R, De Nicola L, Mallamaci F, Zoccali C. Thiazide diuretics are back in CKD: the case of chlorthalidone. *Clinical Kidney Journal*, 2023 Jan; 16(1): 41-51.
9. Huang X, Dorhout Mees E, Vos P, Hamza S, Braam B. Everything we always wanted to know about furosemide but were afraid to ask. *American Journal*

- of Physiology-Renal Physiology, 2016 May 1; 310(10): F958-71.
10. Pacifici GM. Clinical pharmacology of furosemide in neonates: a review. *Pharmaceuticals*, 2013 Sep 5; 6(9): 1094-129.
 11. Phakdeekitcharoen B, Boonyawat K. The added-up albumin enhances the diuretic effect of furosemide in patients with hypoalbuminemic chronic kidney disease: a randomized controlled study. *BMC nephrology*, 2012 Dec; 13: 1-9.
 12. Garcia Sanchez JJ, Thompson J, Scott DA, Evans R, Rao N, Sörstadius E, James G, Nolan S, Wittbrodt ET, Abdul Sultan A, Stefansson BV. Treatments for chronic kidney disease: a systematic literature review of randomized controlled trials. *Advances in Therapy*, 2022 Jan; 39(1): 193-220.
 13. Carone L, Oxberry SG, Twycross R, Charlesworth S, Mihalyo M, Wilcock A. Furosemide. *Journal of Pain and Symptom Management*, 2016 Jul 1; 52(1): 144-50.
 14. Magdy JS, McVeigh J, Indraratna P. Diuretics in the management of chronic heart failure: when and how. *Australian Prescriber*, 2022 Nov 30; 45(6).